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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte IB MENDEL-HARTVIG, ILYA ZELIKMAN, and GERD RUNDSTROM

Appeal 2007-4485
Application 09/582,734
Technology Center 1600

Decided: August 29, 2008

Before, TONI R. SCHEINER, DEMETRA J. MILLS, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. Claims 1-4 and 6-35 are pending. The Examiner has rejected the claims for anticipation and obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

The following claims are representative.

1. A method for determination of an analyte in a sample in a flow matrix by use of a transport flow of one or more biospecific affinity

reactants, at least one of which is analytically detectable (Reactant*) and one of which is firmly anchored in the matrix
(Reactant I), and the flow matrix comprises:

A) an application zone adapted for application of liquid (LZ), which liquid contains buffer and sample and optionally reactants needed for a complete determination, but not Reactant I,

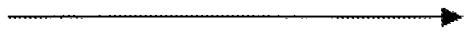
B) a detection zone (DZ) with the firmly anchored reactant (Reactant I) located downstream of LZ, and

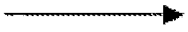
C) optionally one or more zones in which any of the reactants needed for a complete determination, but not Reactant I, has been pre-deposited,

wherein (i) the flow towards the detection zone is initiated by addition of the liquid with sample in the application zone LZ for transport of analyte and reactants towards the detection zone (DZ), and (ii) the amount of the Reactant* bound to DZ is detected, wherein the detected amount is correlated to the amount of analyte in the sample, wherein

I. the flow matrix comprises at least two application zones for liquid LZ arranged substantially adjacent to each other:

$LZ_m, \ldots LZ_n, \ldots LZ_1$ DZ



flow direction 

wherein

a) LZ_n is an application zone for liquid, and n is the position of the application zone LZ_n,

b) m is the total number of application zones in which flow is initiated, m is greater than or equal to 2, and m is not equal to n, wherein LZ_m, is the farthest upstream liquid application zone,

c) one LZ_n, is an application zone for sample (LZ_n,S) and one LZ_n is for

Reactant* (LZ_n,R*) with n" $\geq$ n';

d) ⟶ is the direction of the flow, and

e) DZ is the detection zone, and

II. flow is initiated by adding liquid to each zone LZ_m. . LZ_n. . LZ_1 in such a way that liquid $_{n+1}$, added to the application zone LZ_{n+1},contacts the flow matrix substantially simultaneously with and is transported through the matrix immediately after liquid $_n$, added to the nearest downstream application zone LZ_n.

12. The method according to claim 1, wherein at least one reactant, other than Reactant*, is pre-deposited in an application zone LZ_n ... R for liquid intended for transport of the reactant.

15. The method according to claim 1, wherein the matrix comprises at least one calibrator zone (CZ), in which calibrator is bound to, or in advance has been bound to the matrix.

17. The method according to claim 1, wherein the method is performed as part of diagnosing allergy or autoimmune disease.

34. The method according to claim 10, wherein each zone spacer comprises a strip attached to the flow matrix.

Cited References

Self et al.	4,446,231	May 1, 1984
Dafforn et al.	4,981,786	Jan. 1, 1991
Robinson et al.	WO 95/16914	Jun. 22, 1995
Goerlach-Graw et al.	5,556,789	Sep. 17, 1996

Grounds of Rejection

1. Claims 1, 3, 7, 9, 10, 13, 14, 18, 20, 21, 24, 25, 27, 28 and 32 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Dafforn.

2. Claims 2, 4, 6, 8, 11, 19, 22 and 23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dafforn.

3. Claims 12, 15, 16, 26, 29 and 30 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dafforn in view of Robinson.

4. Claims 17 and 31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dafforn in view of Self.

5. Claims 34 and 35 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dafforn in view of Goerlach-Graw.

DISCUSSION

Background

> "The invention relates to a method for determination of an analyte in a sample by use of biospecific affinity reactants (Reactant 1, Reactant 2 etc.), one of which is analytically detectable (Reactant*) and one is firmly anchored in a detection zone in a transport flow

> matrix (Reactant I). The sample (analyte) is transported by a flow in the matrix from one application zone for liquid (LZS) containing the analyte (sample) and/or a buffer, to the detection zone (DZ), in which Reactant I is firmly anchored. At the same time as the sample is transported in the matrix the soluble reactants, including Reactant*, are also being transported. In the detection zone Reactant* is captured in an amount which is related to the amount of analyte present in the sample. To achieve this, Reactant* is chosen so that it may bind biospecifically directly to Reactant I or indirectly via one or more added biospecific affinity reactants (including the analyte). The amount of analyte is then determined from the amount of Reactant* bound in the detection zone. The transport flow may contain zones, in which different biospecific affinity reactants (e.g. Reactant*, but not analyte) have been applied in advance (predeposited) in order to be dissolved and transported along with the flow towards the detection zone."

(Spec. 1.)

The Specification further indicates that

> if flow is initiated by almost simultaneous addition of liquid to two adjacent zones in a flow marrix, liquid added in the downstream zone migrates before the liquid which has been added_in the upstream zone in a direction towards the detection zone. Our discovery involves that zonewise migration of liquids may also be obtained if addition of liquid in an upstream zone is performed after addition of liquid in the nearest downstream zone.

(Spec. 4.)

1. Claims 1, 3, 7, 9, 10, 13, 14, 18, 20, 21, 24, 25, 27, 28 and 32 stand rejected under 35 U.S.C. § 102(b) as being unpatentable over Dafforn. Each separately argued claim has been addressed in the Answer.

The Examiner finds that:

> Dafforn et al disclose an immunoassay device and method for determining an analyte in a sample. Dafforn et al also disclose that the device comprises a bibulous material which is susceptible to traversal by an aqueous medium in response to capillary force (flow matrix), (col 7, lines 8-10). Dafforn et al disclose that the device may be used in assays wherein absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for analyzing for the analyte (col 4, lines 10-16). Dafforn et al disclose the device comprises a first means for introducing a sample into the device and second means other than the first means for introducing a liquid reagent other than the sample into the device (col 3, lines l-20). Dafforn et al disclose that the liquid reagent can be an ancillary reagent such as a buffer or a labeled reagent (Reactant*). Dafforn et al disclose that the labeled reagent can be provided as liquid reagent or predeposited (col 19, line 15 - col 20, line 22). Dafforn et al disclose that the liquid reagent can be added upstream of the test solution (sample) (col 18, lines 27-29). Dafforn et al also disclose that both of these application zones are located upstream of an immunosorbing zone (detection zone) and that specific binding members (antibodies) (Reactant I) are immobilized in the immunosorbing zone (col 18, line 3 - col 19, line 48). … Dafforn et al also disclose that the sample may be introduced before the liquid reagent if so desired (col 18, lines 20-32)….. Dafforn et al also disclose that the application of liquid can be performed simultaneously in the application zones (col 24, lines 30-32). Dafforn et al also disclose that the reagents can be predeposited in the matrix.

(Ans. 3-4.)

Appellants contend that they:

> find no teaching or suggestion by Dafforn et a1 relating to a method or device as presently claimed wherein at least one

> biospecific affinity reactant (Reactant I) is firmly anchored in the flow matrix and at least one biospecific affinity reactant is applied to an application zone in combination with a flow matrix arrangement as recited in claims 1 and 18. Particularly, Appellants find no teaching or suggestion by Dafforn et a1 of a method or device wherein flow is initiated by adding liquid to each zone in such a way that liquid $_{n+1}$ added to the application zone LZ $_{n+1}$ contacts the flow matrix substantially simultaneously with and is transported through the matrix immediately after liquid $_{n}$, added to the nearest downstream application zone LZ $_{n}$.
>
> Appellants conclude that
>
> the only specific mention of simultaneous application which Appellants find in the teachings of Dafforn et a1 is at column 24, beginning at line 22 wherein an assay is described as conducted by adding a sample suspected of containing human chorionic gonadotrophin (HCG) at a first opening and simultaneously adding a developer solution at the second opening. However, contrary to the present methods and device wherein liquid $_{n+1}$ added to the application zone LZ $_{n+1}$ contacts the flow matrix *substantially simultaneously* with and is transported through the matrix *immediately after* liquid $_{n}$, added to the nearest downstream application zone LG $_{n}$, Dafforn et a1 disclose that the sample HCG binds to an enzyme conjugate and the resulting complex, namely of HCG and enzyme conjugate, is carried *by the moving developer solution* to the detection zone where it binds, i.e., where the HGC-enzyme conjugate complex binds to the detection zone.

(App. Br. 11.) Thus Appellants argue that the ordinary meaning of the phrase "immediately after" in the claim excludes mixing or carrying of liquid. (Reply Br. 3.)

We agree with the rejections and responses to Appellants' arguments that are set out in the Examiner's Answer, and therefore adopt the Examiner's reasoning as our own.

In particular, we agree with the Examiner that

> The claims are not limited to a method where the labeled reagent is moving in a separate front, i.e. behind a sample liquid. Instead, the claims recite an embodiment where the labeled reactant is located in the same zone where sample is added, (i.e. LZ_n"R* and LZ, with n" $\geq$ n'), since n is recited as the position of the application zone (LZ,), the indication that n" is $\geq$ n' is interpreted as an embodiment where the sample application zone and the zone for the labeled reactant is the same, i.e. Dafforn, column 24, lines 23-46. In this case, a complex between the analyte and the labeled reactant is formed when sample is added to LZ_n, and this complex is moving in front of any liquid that is added to the other liquid addition zones. Because the claims do not make clear what "liquid" may be added to the various zones, this "liquid" could be buffer or substrate solution, in which case, after the complex of Dafforn reaches the detection zone, the bound complex acts on any substrate solution that subsequently enters the detection zone, resulting in a color change. These teachings are seen to be the same as those of the instant claims.

(Ans. 9-10.)

We also agree that with the Examiner's claim interpretation that

> the instantly recited claims do not exclude any mixing or carrying. The instantly recited claims only requires that flow is initiated by adding liquid to each zone in such a way that $liquid_{n+1}$, added to the application zone LZ_{n+1}, contacts the flow matrix substantially simultaneously with and is transported through the matrix immediately after liquid, added to the nearest downstream application zone LZ_n. There is no recitation excluding any mixing or carrying or that all reagents and

> sample reach the detection zone in the exact same order without any mixing or carrying.

(Ans. 11-12.) We further find that the ordinary meaning of the term "immediately" means "instantly; with no time intervening; or near or close by."[1] The ordinary meaning of the term "after" means "behind in place or order."[2] Thus, giving the claim language its broadest reasonable interpretation, we conclude that with no time intervening between, or a nearness of liquid $_{n+1}$ transported through the matrix immediately after, or close by to liquid $_{n}$, one of ordinary skill in the art would conclude from the closeness of the liquids in the flow matrix that there is the potential for mixing between the liquids. Appellants point to no teaching in the Specification which precludes mixing or carrying of the liquids, as claimed.

The Answer has responded to each of Appellants arguments for each separately argued claim in the Brief and reiterated in the Reply Brief. Again, we agree with the rejections and responses to Appellants' arguments that are set out in the Examiner's Answer at pages 8-13, and therefore adopt the Examiner's reasoning as our own.

The Examiner's rejection is affirmed.

2. Claims 2, 4, 6, 8, 11, 19, 22 and 23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dafforn. Each separately argued claim has been addressed in the Answer.

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[1] http://www.thefreedictionary.com/immediately

[2] http://www.thefreedictionary.com/after

The Examiner finds that:

> Dafforn et al differ from the instant invention in failing to specifically teach n">n' wherein Reactant*, is upstream of a liquid application zone for sample and the liquids are applied substantially simultaneously to the flow matrix.
> Dafforn et al is silent with respect to substantially simultaneously adding Reactant*, upstream of liquid application zone for sample. However, Dafforn et al specifically teach that the Reactant* can be applied upstream of the liquid application zone for sample. Dafforn et al also disclose many embodiments regarding Reactant* in which Reactant* is applied upstream of the application zone of sample or to the same zone as the sample. Although, Dafforn teaches that when (Reactant*) is added upstream of sample, that the liquid reagent usually is added following the addition of sample (col 13, lines 32-44), Dafforn also teaches the addition of liquid reagents simultaneously (col 24). Therefore, it would have been obvious to one of ordinary skill in the art to add Reactant* upstream of a liquid application zone for sample and to apply the liquids simultaneously in order to optimize assay conditions. Further, it is well settled that a reference must be evaluated for all disclosures not just its preferred embodiments. In re *Mills,* 470 F. 2d 649, 176 USPQ 196 (CCPA 1972).

(Ans. 5-6.)

Appellants contend that "Dafforn et al provide no teaching or suggestion of a method or device employing such a structure of liquid application zones or of providing sequential transport of simultaneously applied liquids." (App. Br. 18-20.)

As set forth herein, we agree with the rejections and responses to Appellants' arguments in the Brief and Reply Brief that are set out in the Examiner's Answer at pages 14-16, including those to the separately argued

claims and therefore adopt the Examiner's reasoning as our own. The rejection is affirmed.

3. Claims 12, 15, 16, 26, 29 and 30 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dafforn in view of Robinson. We select claim 1 as representative of the rejection before us since Appellants have not separately argued the claims. 37 C.F.R. 41.37(c)(1)(vii).

The Examiner finds that:

> Dafforn et al differ from the instant invention in failing to specifically teach n">n' wherein Reactant*, is upstream of a liquid application zone for sample and the liquids are applied substantially simultaneously to the flow matrix.
>
> Dafforn also fails to teach a calibration zone as in Claim 15.

To make up for these deficiencies, the Examiner relies on Robinson which discloses

> the use of calibration zone(s), in which a calibration reagent is immobilized and has biospecific affinity for the analyte of interest or the binding partner of interest (page 15, lines 15-24). Robinson et al also disclose a releasable reagent predeposited (abstract). Robinson et al also disclose that the device may be a flow through device such as test strip (page 5, lines 7-22). Robinson et al also disclose that the specific binding partner can be coupled to or conjugated to the calibrator (see page 17), to form a complex for detection. Robinson et al disclose that the reagents may be antigen/antibody complexes. Robinson et al disclose that calibrator zones used in this manner offers means for calibrating the assay as part of the assay procedure (page 3, lines 15-1 6) and also provides advantages for additional compensation for various factors in the assay system which may influence the level of signal observed (page 14, lines 24-26).

(An. 6-7.)

Dafforn teaches that multiple reagents may be used and that the reagent can be predeposited. (Dafforn, col. 19, l. 5 to col. 20, l. 22.) Robinson teaches that a reactant other than Reactant*, such as a calibrator, is predeposited. (Robinson, abstract.)

The Examiner concludes that:

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the use of a calibrator zone as taught by Robinson et al into the method and device of Dafforn et al because Robinson et al disclose that calibrator zones used in this manner offers means for calibrating the assay as part of the assay procedure (page 3, lines 15-16) and also provides advantages for additional compensation for various factors in the assay system which may influence the level of signal observed.

(Ans. 7.)

Appellants argue that:

> [They] find no teaching or suggestion by Dafforn et a1 relating to an additional zone $LZ_{n"}R$ as presently required by claims 12 and 26, or relating to calibration, particularly, integral with their device, or relating to a calibration zone in their device, calibrator predeposited in or applied to a matrix, or a binder for a calibrator in a calibration zone, as required by claims 15, 16, 29 or 30.

(App. Br. 23.)

Appellants further argue that the

> deficiencies of Dafforn et a1 are not resolved by Robinson et al. Robinson et a1 describe a sensor device for a sandwich assay comprising a discrete zone having a measurement region on

> which is immobilized a first specific binding partner for a ligand under assay and a known amount of a releasable optionally labeled second specific binding partner for the ligand under assay, and a second discrete zone having a region on which is immobilized a first specific binding partner for the ligand under assay, a releasable known amount of ligand analog, and a second known amount of a second optionally labeled second specific binding partner for the ligand under assay.

(App. Br. 23.)

We agree with the rejections and responses to Appellants' arguments that are set out in the Examiner's Answer at pages 16-17, and therefore adopt the Examiner's reasoning as our own. The rejection is affirmed.

4. Claims 17 and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn in view of Self. We select claim 17 as representative of the rejection before us since Appellants have not separately argued the claims. 37 C.F.R. 41.37(c)(1)(vii).

According to the Examiner:

> Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune diseases. Self et al. shows that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to use immunoassays as taught by Self et al. for the diagnosis of autoimmune diseases because Self et al. shows that immunoassays are used for the detection and/or determination of autoimmune diseases and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any

> circumstance where it is necessary to detect and/or determine small or very small amounts of substances. Therefore, it would have been obvious to one of ordinary skill in the art to use the device and method of Dafforn et al for diagnosing autoimmune disease.

(Ans. 7-8.)

Appellants contend that they:

> [F]ind no specific teaching or suggestion by Dafforn et a1 relating diagnosing allergy or autoimmune disease. The deficiencies of Dafforn et a1 are not resolved by Self. That is, while Self discloses an immunoassay using an amplified cyclic detection system, Appellants find no teaching or suggestion by Self relating to a method or device for determination of an analyte in a sample and a flow matrix employing a combination of biospecific affinity reactants and liquid application zones and flow as defined in claims 1 and 18. Similarly, Appellants find no teaching or suggestion by Self for modifying any of the teachings of Dafforn et a1 to result in either a method or a device as presently claimed. Thus, the mere teaching by Self of the use of immunoassays for detection and/or determination of autoimmune diseases does not resolve the deficiencies of Dafforn et al., particularly with respect to a method and device allowing simultaneous liquid application and sequential liquid transport and the advantages of such with respect to diagnosing allergy or autoimmune disease.

(App. Br. 26.)

We agree with the rejections and responses to Appellants' arguments that are set out in the Examiner's Answer at page 17, and therefore adopt the Examiner's reasoning as our own. The rejection is affirmed.

5. Claims 34 and 35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn in view of Goerlach-Graw. We select claim 34 as

representative of the rejection before us since Appellants have not separately argued the claims. 37 C.F.R. 41.37(c)(1)(vii).

The Examiner finds that "Dafforn et al differ from the instant invention in failing to specifically teach wherein each spacer comprises a strip attached to the flow matrix." (Ans. 8.) The Examiner relies on Goerlach-Graw for the disclosure of barriers in the form of strips in a flow matrix.

> "Goerlach-Graw disclose that such barriers can be integrated at any desired position between the sample application zone and the reagent zone (col 6). Goerlach- Graw et al disclose that these barriers provide for a device wherein flooding of the test elements with sample liquid is avoided by using these retardation zones."

(Ans. 8.)

The Examiner concludes that:

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate barriers such as taught by Goerlach-Graw et al into the device and method of Dafforn et al because Goerlach-Graw et al shows that these barriers provide for a device wherein flooding of the test elements with sample liquid is avoided by using these retardation zones.

(Ans. 8.)

Appellant contends that:

> Appellants find no specific teaching or suggestion by Dafforn et a1 relating zone spacers comprising a strip attached to the flow matrix. In fact, placement of spacers between liquid application zones on the flow matrix of Dafforn et a1. would be contrary to the teachings of Dafforn et a1. which desire contact of developer and the analyte-enzyme conjugate complex

> prior to the detection zone.
>
> The deficiencies of Dafforn et al are not resolved by Goerlach-Graw et al. That is, Goerlach-Graw et al disclose a device including three individual test strips extending in parallel from a single application zone. However, Appellants find no teaching in this reference relating to a single flow matrix having liquid application zones in series therein, as required in claims 1 and 18, particularly with spacers in the form of a strip between each zone. While the Examiner refers to column 6, the various embodiments at column 6 are directed to slowing liquid migration in one or more of the strips so that there is simultaneous wetting of the sample withdrawal sites on the respective test strips. This provides no teaching or suggestion of zone spacers as presently claimed between a plurality of liquid application zones in series in a single flow matrix, or for modifying the teachings of Dafforn et al along the lines of the present invention. In fact, such test strips are contrary to promoting contact between developer and conjugate as desired by Dafforn et al.

(App. Br. 27-28.)

We agree with the rejection set out in the Examiner's Answer at page 8, and therefore adopt the Examiner's reasoning as our own. In particular, Dafforn discloses a multiport assay device with two openings or wells. (Fig. 2.) The separated wells in the device housing constitute zone spacers between liquids introduced into the device. Goerlach-Graw discloses the use of constant compression of the fleece or flow matrix material with cross-pieces (8) or strips of housing which face one another or are staggered in the bottom and/or lid component of the housing to retard liquid flow. (Goerlach-Graw, col. 6, ll. 10-18.) Alternatively, Goerlach-Graw indicates that a paper or membrane (strip) can be incorporated into the transport path or flow matrix between the sample application zone and the first reagent zone to act as a hydrophobic barrier. (Goerlach-Graw, col. 6, ll. 27-39.) We

further agree with the Examiner that the claim language "zone spacer comprises a strip attached to the flow matrix" does not exclude a housing strip or paper or membrane strip, as disclosed in Goerlach-Graw. The rejection is affirmed.

CONCLUSION

The anticipation and obviousness rejections of the Examiner are affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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